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## SEROPREVALENCE OF ANTIBODY TO HDV IN NIGERIANS WITH HEPATITIS B VIRUS-RELATED LIVER DISEASES

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### ABSTRACT

**Objective:** Hepatitis D Virus (HDV) infection has been reported to be declining in some geographical areas. In order to ascertain the current status of HDV infection in Nigeria, a study of patients with hepatitis B virus (HBV)-related liver diseases was undertaken to determine the sero-prevalence of anti-HDV.

**Method:** This was a prospective, cross-sectional study in which all consecutive patients with liver disease who tested positive for Hepatitis B surface antigen (HBsAg) were also tested for antibody to HDV.

**Result:** Ninety six patients with various forms of HBV-related liver diseases participated in the study (acute hepatitis 8.3%, asymptomatic infection 15.6%, chronic hepatitis 3.1%, liver cirrhosis 21.9% and primary liver cell carcinoma 51.0%). Anti-HDV was demonstrated in 12 patients (12.5%). In patients with acute hepatitis and asymptomatic infection the prevalence was 4.3% while in patients with chronic hepatitis, liver cirrhosis and primary liver cell carcinoma, the prevalence was 15%.

**Conclusion:** HDV still contributes to significant morbidity and mortality in HBV-related liver diseases in Nigeria. There is urgent need for larger studies on a national scale to accurately appraise the public health importance of this infection.

**Key Words:** Hepatitis D Virus, Hepatitis B Virus, Sero-prevalence. (Accepted 7 October 2008)

### INTRODUCTION

The hepatitis delta virus (HDV) is a defective RNA virus dependent on Hepatitis B virus (HBV) infection for its replication and expression<sup>1,2</sup>. Infection with HDV can occur simultaneously with acute HBV infection (coinfection) or may be superimposed on chronic infection (superinfection)<sup>3</sup>. It is known that coexistent infection with HDV tends to accelerate the progress of chronic HBV infection to chronic hepatitis, cirrhosis and hepatocellular carcinoma<sup>4</sup>. Fulminant hepatitis may develop in 20-30% of patients coinfecting with HBV and HDV but only about 2% of patients with HBV monoinfection experience this complication<sup>5</sup>. Sero-prevalence studies in individuals positive for HBsAg show a non-uniform worldwide distribution of HDV<sup>6</sup>. The regions of the world with highest prevalence of HDV infection are the Mediterranean basin including the Middle East, Eastern Europe, and some regions of Asia<sup>4,7,8</sup>. In Nigeria, the literature is replete with studies on HBV infection in different cohorts<sup>9-16</sup> but not much is known about the prevalence of HDV infection in patients with HBV-related liver diseases. In Western Nigeria two different studies on patients with chronic liver disease showed prevalences of 4% and 6.5%<sup>17,18</sup>.

Some countries of the world have already recorded declining trends in the occurrence of HDV infection<sup>19-21</sup>. The main objective of this study was to determine the current seroprevalence of HDV antibody in patients with various forms of HBV-related liver disease at the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu, South Eastern Nigeria.

### METHOD

This was a prospective, cross-sectional study of consecutive patients with clinical features of liver disease seen at the Gastroenterology Unit, Department of Medicine, University of Nigeria Teaching Hospital (UNTH) Ituku/Ozalla, between April 2006 and September 2006. The study was approved by the UNTH research ethics committee and informed consent was obtained from all the participants. Initial evaluation of the patients included detailed history and thorough physical examination with emphasis on the hepato-biliary system. Each participant had his blood tested for Hepatitis B surface antigen (HBsAg) with an enzyme-linked immunosorbent assay (ELISA) kit that uses polystyrene microwell strips pre-coated with monoclonal antibodies specific to HBsAg. The test has a sensitivity of 99.75% and specificity of 99.63%. Those who tested positive were further tested for

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serum bilirubin (total and fractions), liver enzymes (transaminases, and alkaline phosphatase), serum protein (total and fractions), prothrombin time, full blood count, urinalysis, abdominal ultrasonography and where feasible, liver biopsy. Asymptomatic individuals referred to the gastroenterology unit after testing positive for HBsAg during screening for blood donation or premarital testing were also included and they underwent clinical evaluation and laboratory tests as the other patients. Antibody to HDV was tested for using ELISA kit for qualitative determination of anti-HDV in human serum. The test is based on solid phase, one step incubation competitive ELISA, manufactured by Diagnostics Automation, Inc. California USA. The sensitivity and specificity approach 100%. Based on the clinical features and results of the investigations the patients were grouped into acute hepatitis, asymptomatic HBV infection, chronic hepatitis, liver cirrhosis and hepatocellular carcinoma.

#### Statistical Analysis

The results were analyzed with the computer program SPSS version 13 and expressed as means and proportions. Where appropriate, differences between proportions and means were determined using the chi-square test and t-test. Statistical significance was achieved if  $p=0.05$ .

## RESULT

A total of 132 patients with various forms of liver disease were screened for HBsAg. Ninety six of them (72.7%) tested positive for HBsAg. These were made up of 8 patients with acute hepatitis (8.3%), 15 patients with asymptomatic infection (15.6%), 3 patients with chronic hepatitis (3.1%), 21 patients with liver cirrhosis (21.9%) and 49 patients with primary liver cell carcinoma (51.0%). There were 77 males (80.2%) and 19 females (19.8%). Table 1 illustrates the gender distribution of patients with various forms of HBV-related liver diseases. The mean age of the patients was  $41.14 \pm 18.21$  years. The mean age of the males was  $42.04 \pm 18.96$  years while the mean age of the females was  $37.58 \pm 14.81$  years. The difference between the mean ages of the male and female patients was not statistically significant ( $p = 0.3420$ ). The mean age of patients who had acute hepatitis and asymptomatic infection was  $25.57 \pm 5.84$  years while the mean age of patients with chronic hepatitis, cirrhosis and primary liver cell carcinoma was  $46.26 \pm 17.99$  years. The difference between the means was statistically significant ( $p < 0.0001$ ). Anti-HDV was demonstrated in 12 patients (12.5%), made up of 10 males and 2 females. The gender specific prevalence of anti-HDV was 13.0%

Table 1: Gender Distribution of Patients with HBV Related Liver Diseases.

Liver Disease	Male	Female	Total
Acute Hepatitis	6	2	8 (8.3)
Asymptomatic HB, Ag Positive	12	3	15 (15.6)
Chronic Hepatitis	3	-	3 (3.1)
Liver cirrhosis	16	5	21 (21.9)
Hepatocellular carcinoma	40	9	49 (51.0)
<b>Total</b>	<b>77 (80.2)</b>	<b>19 (19.8)</b>	<b>96 (100)</b>

Figures in parentheses = Percentages

Table 2: HDV Antibody in HB Related Liver Diseases.

Liver Disease	Anti – HDV Positive
Acute Hepatitis, n = 8	0 (0)
Asymptomatic HBS Ag Positive, n = 15	1 (6.7)
Subtotal, n = 23	1 (4.3)
Chronic Hepatitis, n = 3	0 (0)
Liver cirrhosis, n = 21	3 (14.3)
Hepatocellular carcinoma, n = 49	8 (16.3)
Subtotal, n = 73	11 (15.0)
<b>Grand Total = 96</b>	<b>12 (12.5)</b>

Figures in parenthesis = Percentages

for males and 10.5% for females. The difference was not statistically significant ( $p=0.7590$ ). Table 2 illustrates the anti-HDV sero-positivity in the different forms of liver diseases. The prevalence of anti-HDV was 0% in acute hepatitis, 6.7% in asymptomatic infection, 0% in chronic hepatitis, 14.3% in liver cirrhosis and 16.3% in hepatocellular carcinoma. The disease spectrum of HBV infection can be grouped into early disease (acute hepatitis and asymptomatic infection) and late infection (chronic hepatitis, liver cirrhosis and hepatocellular carcinoma). In this study the prevalence of anti-HDV was 4.3% for early disease and 15.0% for late infection. The difference between the proportions was, however, not statistically significant ( $p=0.203$ )

## DISCUSSION

The prevalence of anti-HDV in this study was 12.5%. This cannot be compared directly with the studies in Western Nigeria<sup>17,18</sup> which showed lower prevalence. The latter studies actually assayed HDV antigen while this study assayed anti-HDV. Furthermore, there have been reports of regional variability in HDV prevalence in some parts of Africa<sup>22</sup> and this may also be operative in Nigerian patients. There is need for more studies to further elucidate this. Advanced stages of HBV infection (liver cirrhosis and primary cell carcinoma) accounted for about 73% of the patients with HBV-related liver diseases who participated in this study. This is most likely because of late presentation which is a major problem in virtually all diseases encountered in developing countries. Even when patients are discovered at the stage of asymptomatic infection, follow up is usually a problem, because they often default and only reappear in hospital at a late stage when the chances of cure are almost non-existent. This calls for concerted and sustained efforts at health education of the populace on the need for routine medical checks so that individuals with early stages of the disease can be identified, followed up and prompt interventions instituted as appropriate. The gender-specific prevalence of HDV antibody in this study was 13.0% in males and 10.5% in females. The difference was not statistically significant. This is different from what was observed in the Western Brazilian Amazon where the prevalence is significantly higher in males<sup>23</sup>. The prevalence of anti-HDV in patients with late stages of HBV-related liver diseases (chronic hepatitis, liver cirrhosis and hepatocellular carcinoma) was 15.0% compared to a lower prevalence of 4.3% in patients with early infection (acute hepatitis and asymptomatic infection). Even though the difference was not statistically significant, this might be an important observation because it suggests that superinfection

rather than coinfection may be the dominant mode of HDV infection in these patients. A higher prevalence in the late stages of HBV-related liver disease was also reported in a study in Turkey<sup>19</sup>. Some countries have already recorded declining trends in the occurrence of HDV infection<sup>19,21</sup>. This is sequel to the introduction of childhood immunization against HBV as part of national immunization programmes. The same cannot be said to apply to most developing countries due to belated or lack of introduction of HBV vaccine in national immunization programmes as well as poor sustainability of such programmes<sup>24</sup>.<sup>26</sup> In Nigeria, the absence of accurate statistical data on the current magnitude of the problem of HDV infection is likely to hamper effective surveillance of this disease. This calls for larger studies on a national scale so that our sub-region is not left out of the current global efforts to stamp out liver diseases caused by viruses.

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